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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,905	03/08/2004	Bruce A. Edgar	14538A-007510US	1659

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/796,905	EDGAR ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26,30-32,35 and 36* is/are pending in the application.

4a) Of the above claim(s) *30,35 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,26,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks filed 12/06/07 are acknowledged.

2. Applicant's substitute Abstract and Title filed 12/06/07 have been entered and the objections have been withdrawn.

3. Claims 1-24, 27-29, 33, 34, and 37-42 have been cancelled.

Claims 30, 35, and 36 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

Claims 25, 26, 31, and 32 are under examination.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 25, 26, 31, and 32 stand rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

As set forth previously, The omitted steps comprise a lack of an adequate correlation step in any of the claims. Regarding Claim 25, the claim lacks a correlation step relating to the preamble of the claim, i.e., there is no recitation of how the measured change in Rheb activity, e.g., increased or decreased, results in the identification of a lead compound for drug development. Regarding Claim 31, the claim fails to recite whether or not the inhibiting of Rheb activity is a positive or negative indicator of a candidate compound for the treatment of a disease associated with abnormal cell growth.

Applicant's arguments, filed 12/06/07, have been fully considered but are not found persuasive. Applicant argues that amendments to the claims have obviated the rejections.

A review of Claim 25 shows that the claim still does not result in the identification of a compound that decreases Rheb activity as set forth in the preamble. The claim results only in an "association" with a reduction in Rheb activity. Likewise, the result of Claim 31 is not the identification of a compound that decreases Rheb activity but rather a step that

requires an undescribed "determining" step to identify an Rheb antagonist.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 25, 26, 31, and 32 stand are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

As set forth previously, Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of a "Rheb protein" other than human or drosophila.

An adequate written description of the Rheb proteins of the claims would require either an adequate description of a common structure and function, or a disclosure of a representative number of Rheb species. While some attempt is made at disclosing a common function, , e.g., the proteins are disclosed as Ras-like, there is no discussion of a common structure. A review of the specification discloses just two species of Rheb protein, human or drosophila (paragraph 12). Given the distant relationship between humans and drosophila, it is clear that there are at minimum millions of Rheb species. Given these facts, one of skill in the art would conclude that the specification fails to disclose either a representative number of species, or common functional and structural characteristics, adequately to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

Applicant's arguments, filed 12/06/07, have been fully considered but are not found persuasive. Applicant argues that the Rheb proteins of the claims are adequately described.

While accession numbers for certain Rheb proteins are disclosed, the specification fails to disclose the common structural and functional features of these Rheb proteins that are expressed by not only mammals and insects, but even fungi.

Also, at page 10 the specification discloses that the term "Rheb protein" encompasses fragments, derivatives, and analogs of Rheb proteins, none of which have been described.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 25, 26, 31, and 32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 03/016499 in view of Yamagata et al. (1994, IDS) and U.S Patent No. 6,986,993.

As set forth previously, WO 03/016499 teaches the assay for the identification of lead compounds (including libraries of compounds), for the inhibition of human Ras, said inhibitors being candidates (e.g., lead compounds) for the treatment of cancer (e.g., a disease associated with abnormal cell growth) (see particularly pages 28-29).

The reference differs from the claimed invention in that it does not teach the screening for inhibitors of Rheb nor the screening by the measurement of cell size.

Yamagata et al. teaches Rheb is a growth factor of the Ras family that is closely related to Ras with the same GTPase activity as Ras (see particularly the Discussion beginning at page 16336).

The '993 patent teaches that cell size can be used for the determination of compounds that affect the viability and metastasis of cancer cells (see particularly Example 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform the method of screening for anti-cancer drugs of WO 03/016449, substituting Rheb for Ras, given the teachings of Yamagata et al. that Rheb is a growth factor of the Ras family that is closely related to Ras with the same GTPase activity as Ras. Because of the similarities between Ras and Rheb, and Ras being known as a target for anti-cancer treatments, the skilled artisan would have been motivated to screen for Rheb inhibitors as possible anti-cancer drugs as well. The skilled artisan would also have been motivated to employ the method by determining cell size given the teaching of the '993 patent that cell size can be measured for the determination of compounds that affect the viability and metastasis of cancer cells.

Applicant's arguments, filed 12/06/07, have been fully considered but are not found persuasive. Applicant argues that

Yamagata et al. fails to teach that Rheb is associated with cancer.

Applicant has provided merely speculation as to differences between Ras and Rheb. In many ways, given the demonstrated homology between the proteins, the differences between the proteins provide the ordinarily skilled artisan as much motivation for their study as do the differences. And in addition to the motivation of pursuing Rheb inhibitors as possible anti-cancer agents, the primary reference, Yamagata et al. provides additional reasons for developing Rheb inhibitors. See the final paragraph of the *Discussion* wherein the authors suggest that Rheb plays a role in processes including cell proliferation and differentiation, vesicular transport, cell polarity, cytoskeletal integrity, scaffolding of actin monofilaments, and *in vitro* NADPH oxidase activation, any or all of which the skilled artisan would be interested in developing tools for manipulating.

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, Ph.D. can be reached on (571) 272-0878.

13. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

2/16/08

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